Speaker: Mark Canfield, Ph.D.

Topic: The Prevalence and Patterns of Neural Tube Defects in Texas

Objectives:

1) Name three birth defects in the category of neural tube defects.
2) Compare Texas rates with U.S. rates
3) Identify one or more Texas regions where neural tube defects are more prevalent
4) Describe the ethnic and socioeconomic patterns of neural tube defects in Texas.

Outline:

1) Neural Tube Defects: Background
2) Prevalence of NTDs in Texas vs. Other Locations
3) Patterns of NTD in Texas
    a) By race/ethnicity
        i) By maternal age
        ii) By sex of infant
        iii) By maternal educational attainment
        iv) By country of birthplace/origin
        v) By area of residence
        vi) Other
4) Summary
5) Current efforts to reduce the impact of NTDs in Texas

Abstract: The first several years of data on neural tube defects (anencephaly, spina bifida, and encephalocele) are now available from the Texas Birth Defects Registry, representing 412,333 live births and many of the regions in Texas. The 1995-97 prevalence for anencephaly, spina bifida, and encephalocele was 3.78, 5.29, and 1.24 per 10,000 live births, respectively. This results in a combined NTD prevalence of approximately 1 case per 1,000 live births, which is the commonly reported NTD birth prevalence for the U.S. Of the 425 cases, 31 cases (7.3%) were considered syndromic or chromosomal in etiology. Only 1/4 of anencephaly cases were live born; most of the remainder were electively terminated. In contrast, over 3/4 of spina bifida cases were live born. For both anencephaly and spina bifida, the highest rate was recorded for the youngest mothers (<20 years of age). For anencephaly, we observed a decreasing prevalence with each older age group. Females had a higher prevalence than males for all three NTD categories. However, for anencephaly, this female excess was observed only for Hispanics. Anencephaly and spina bifida rates were lowest in African-Americans and highest in Hispanics. However, the ethnic differences were most pronounced for spina bifida. Hispanics with the highest rates were those who lived on the border with Mexico or with the lowest educational attainment. Hispanic mothers born in Mexico had rates similar to those born in the U.S. Spina bifida risk decreased with each increasing level of maternal educational attainment. For mothers with more than a high school education, there was no difference in spina bifida rates between Hispanics and non-Hispanics. Relative to other areas of Texas, it appears that Region 8 (San Antonio) had the lowest NTD rate (5.66 cases per 10,000 live births), and the highest rates were recorded in Region 11 (12.90 for the areas of Harlingen/Brownsville/ McAllen/ Laredo/Corpus Christi) and Region 2 (13.65 for the areas including Abilene and Wichita Falls). Rates for anencephaly and especially spina bifida were higher in residents of counties bordering Mexico, compared to non-border residents of Texas.

The Prevalence and Patterns of Neural Tube Defects in Texas

Mark A. Canfield, Ph.D.
Mathias Forrester, B.S.

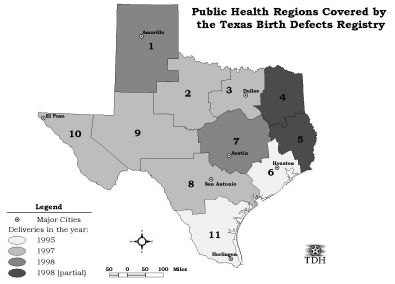
Definitions

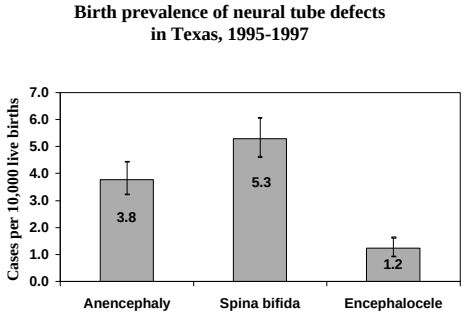
- **Neural Tube Defect** - failure of the neural tube to close at level of brain or spinal cord
- **Anencephaly** - partial or complete absence of brain
- **Spina bifida** - incomplete closure of spinal cord, often with protruded or exposed tissue
- **Encephalocele** - protruded brain tissue

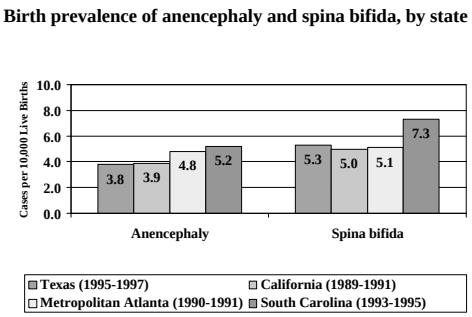
Case Definition

- Cases among live births, fetal deaths (20+), elective terminations (any gestational age)*
- Diagnosed prenatally or in first year of life
- Delivered in 1995*, 1996, or 1997
- Residence in Registry area at delivery
- Co-occurring NTDs counted once

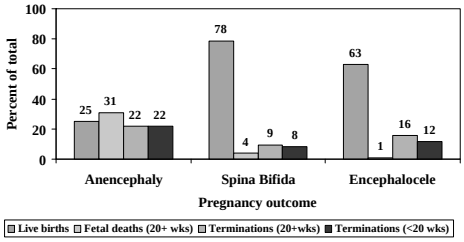
*DIFFERENT FROM PUBLISHED REGISTRY DATA





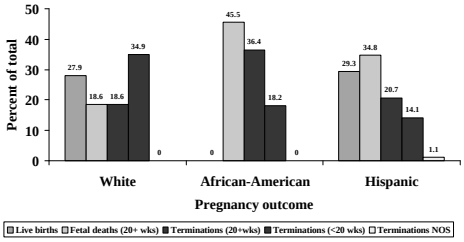


Distribution of neural tube defects in Texas, by pregnancy outcome, 1995-1997



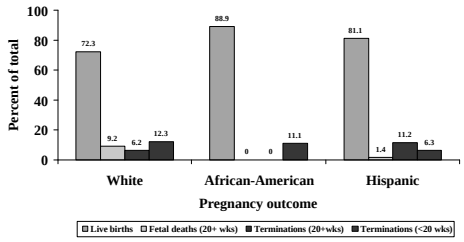
Texas Birth Defects Registry, January 2000

Distribution of anencephaly by pregnancy outcome and maternal race/ethnicity, Texas, 1995-1997



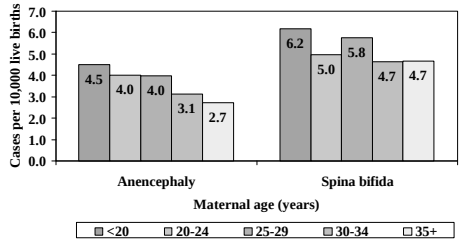
Texas Birth Defects Registry, January 2000

Distribution of spina bifida by pregnancy outcome and maternal race/ethnicity, Texas, 1995-1997



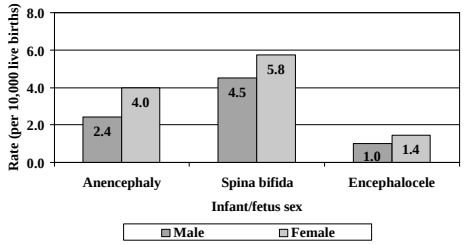
Texas Birth Defects Registry, January 2000

Birth prevalence of anencephaly and spina bifida in Texas by maternal age, 1995-1997



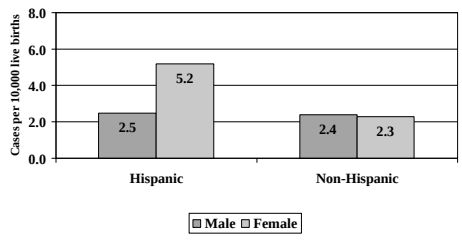
Texas Birth Defects Registry, January 2000

Birth prevalence of neural tube defects in Texas, by infant/fetus sex, 1995-1997



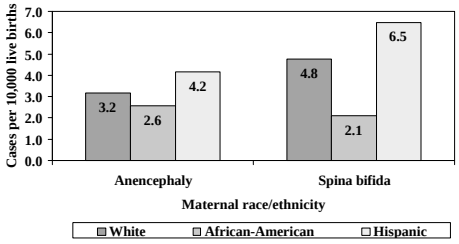
Texas Birth Defects Registry, January 2000

Birth prevalence of anencephaly in Texas, by infant/fetus sex and maternal ethnicity, 1995-1997



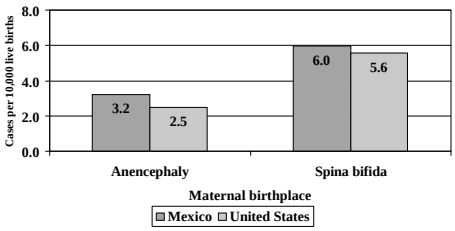
Texas Birth Defects Registry, January 2000

Birth prevalence of anencephaly and spina bifida in Texas, by maternal race/ethnicity, 1995-1997



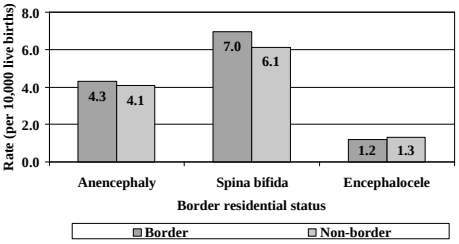
Texas Birth Defects Registry, January 2000

Birth prevalence of anencephaly and spina bifida in Texas Hispanics, by maternal birthplace, 1995-1997



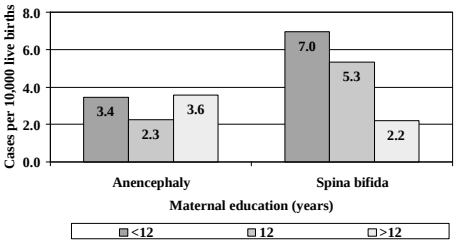
Texas Birth Defects Registry, January 2000

Prevalence of neural tube defects in Texas Hispanics, by border residential status, 1995-1997



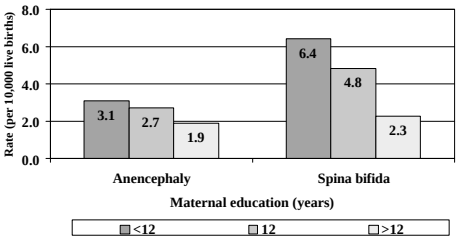
Texas Birth Defects Registry, January 2000

Prevalence of anencephaly and spina bifida in Texas Hispanics, by maternal education, 1995-1997



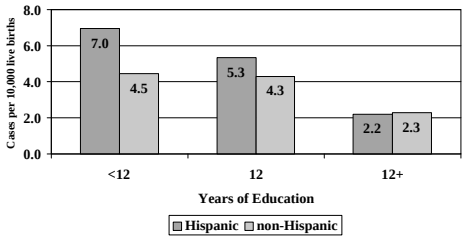
Texas Birth Defects Registry, January 2000

Birth prevalence of anencephaly and spina bifida in Texas, by maternal education level, 1995-1997



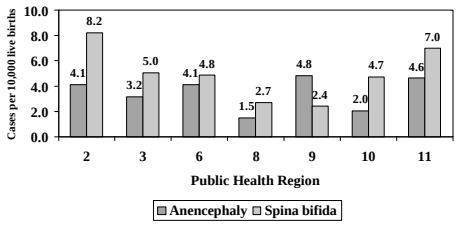
Texas Birth Defects Registry, January 2000

Birth prevalence of spina bifida in Texas, by maternal education and ethnicity, 1995-97



Texas Birth Defects Registry, January 2000

Birth prevalence of anencephaly and spina bifida in Texas, by public health region, 1995-1997

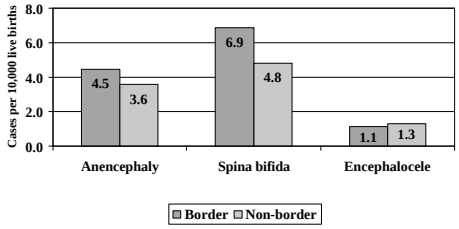


Texas Birth Defects Registry, January 2000

Birth prevalence of anencephaly and spina bifida in Texas, by public health region, 1995-1997

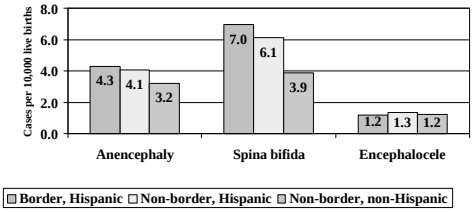
Texas Birth Defects Registry, January 2000

Birth prevalence of neural tube defects in Texas, by border residential status, 1995-1997



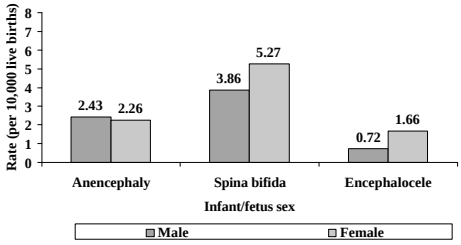
Texas Birth Defects Registry, January 2000

Birth prevalence of neural tube defects in Texas, by border residential status and ethnicity, 1995-1997



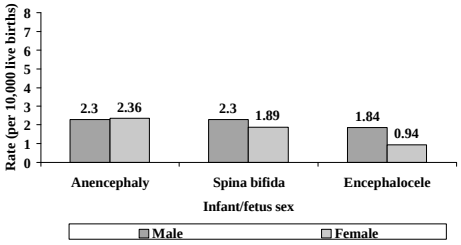
Texas Birth Defects Registry, January 2000

Prevalence of anencephaly, spina bifida, and encephalocele by infant/fetus sex for white mothers, Texas, 1995-1997



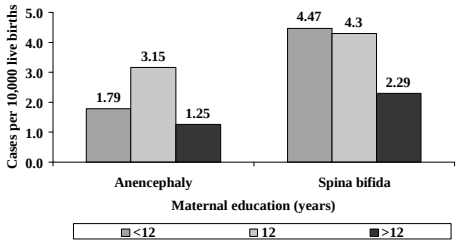
Texas Birth Defects Registry, January 2000

Prevalence of anencephaly, spina bifida, and encephalocele by infant/fetus sex for African-American mothers, Texas, 1995-1997



Texas Birth Defects Registry, January 2000

Prevalence of anencephaly and spina bifida by maternal education for non-Hispanic mothers, Texas, 1995-1997



Texas Birth Defects Registry, January 2000

Conclusions

- Overall NTD prevalence = 1 per 1,000 births (similar to U.S.); rates for spina bifida higher than for anencephaly
- Different patterns for anencephaly, spina bifida, and encephalocele
- Highest rates in Hispanics, border residents, and those with the least education (especially spina bifida)

Texas Birth Defects Registry, January 2000

Limitations

- Data overrepresented by Rio Grande Valley and Hispanics
- Different regions, different time periods
- Missing some electively terminated anencephaly cases?

Strengths

- Population-based active surveillance
- Large # live births
- Includes early and late elective terminations
- Data comparing border vs. non-border
- Multi-ethnic

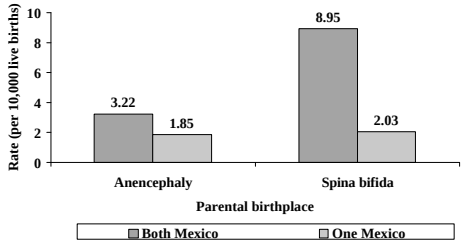
Texas Birth Defects Registry, January 2000

Next Steps & New Developments

- NTD occurrence prevention
  - Texas Folic Acid Council
  - Statewide provider education project (with Research Center, UTSPH-Houston)
- NTD recurrence prevention
  - Statewide intervention project (with Research Center, UTHSC-San Antonio)
- Birth defects project with Texas and 4 bordering Mexican states

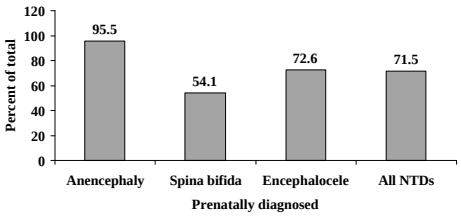
Texas Birth Defects Registry, January 2000

Prevalence of anencephaly and spina bifida by maternal and paternal birthplace for Hispanic mothers, Texas, 1995-1997



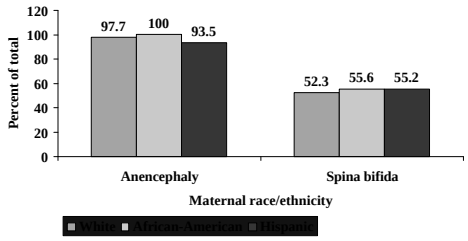
Texas Birth Defects Registry, January 2000

Proportion of neural tube defects that were prenatally diagnosed, Texas, 1995-1997



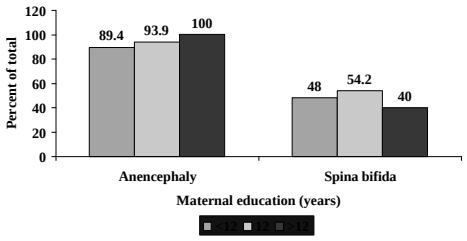
Texas Birth Defects Registry, January 2000

Proportion of anencephaly and spina bifida that were prenatally diagnosed by maternal race/ethnicity, Texas, 1995-1997



Texas Birth Defects Registry, January 2000

Proportion of anencephaly and spina bifida that were prenatally diagnosed by maternal education, Texas, 1995-1997



Texas Birth Defects Registry, January 2000

Speaker: Mark Canfield, Ph.D.

Topic: Patterns of Folic Acid Awareness and Daily Supplementation in Texas

Objectives:
1) Describe the purpose of the Texas Women=s Health Survey.
2) Characterize the risk reduction for neural tube defects by folic acid.
3) Describe three target groups or areas in Texas for neural tube defect prevention.

Outline:
1) Texas Birth Defects Research Center
2) Folic acid and the prevention of NTDs
   a) Recommendations
   b) Occurrence vs. recurrence prevention
   c) Ways to increase folic acid intake
3) Texas Women's Health Survey: Overview, purpose, features
4) Patterns of folic acid awareness in Texas
5) Patterns of folic acid supplementation in Texas
6) Target groups and areas for prevention of NTDs

Abstract: Mark A. Canfield, Dawna Wright, Emily Kahn, Mary Ethen, Jim Dyer. Numerous studies have demonstrated that 400 micrograms of the vitamin folic acid as a daily supplement can prevent 50-70% of all cases of neural tube birth defects (anencephaly and spina bifida). However, it must be taken prior to closure of the neural tube (3-4 weeks after conception), before most women know they are pregnant. This is why the U.S. government and Texas Department of Health have recommended since 1992 that *all women of childbearing potential* consume 400 micrograms folic acid daily. In the Fall of 1997, a CDC-funded statewide telephone survey was conducted for the Texas Birth Defects Research Center that focused on the awareness and practices relating to folic acid and the prevention of birth defects. From a sample of nearly 1,300 women of childbearing age in Texas, 66% reported having Aread or heard something about folic acid,@ which was identical to the national awareness level from a similar 1997 survey. When asked *what* they had read or heard about folic acid, only 16% of the Texas respondents knew that folic acid prevents birth defects, and only 14% were aware that it should be taken before pregnancy (as recommended). When asked *where* they had heard or read about folic acid, roughly 1/3 of the sample mentioned magazines/newspapers or television/radio, but only 25% mentioned health care provider. Only 1/3 of all respondents reported taking a daily supplement that contained the minimum dose of folic acid (400 micrograms) recommended for women of childbearing age to prevent neural tube defects. Those most likely to take folic acid supplements daily were older, white, more educated, or reported a higher household income. Women in the San Antonio public health region were most likely to consume supplements with folic acid daily (39%), whereas women in the Rio Grande Valley were least likely to supplement (23%). Residents of the 14 counties bordering Mexico reported lower rates of daily supplementation than non-border residents of Texas. This border-non border difference persisted when adjusting for education, but became non-significant when adjusting for race/ethnicity. For those with a college degree, there were no significant differences in supplementation rates between ethnic groups.

Speaker: Joe Mulinare, M.D., M.S.P.H.

Topic: An International Investigation of High Rates of Neural Tube Defects in Northern China

Objectives:

1) Relate the circumstances leading to an investigation of neural tube defects in China
2) Compare the rates of neural tube defects in Northern China, relative to one other country or area.
3) Describe one unique method used in this investigation.
4) Describe an outcome of this investigation.

Abstract: Several provinces in China participated in an evaluation of a folic acid public health campaign conducted from 1993 to 1995. Women were asked to take a pill containing 400 micrograms of folic acid alone daily from the time of their premarital examination until the end of their first trimester of pregnancy. Statistically significant reductions in risk for NTDs occurred among fetuses and infants of women who consumed folic acid periconceptionally. The results from this evaluation demonstrate that the ingestion of 400 micrograms of folic acid alone per day during the periconceptional period prevents neural tube defects. This preventive effect can be observed in both areas of high or low NTD prevalence.

Speaker: Kate Hendricks, M.D., M.P.H. and T.M.

Topic: Selected Findings from a Case-Control Study of Neural Tube Defects on the Texas-Mexico Border

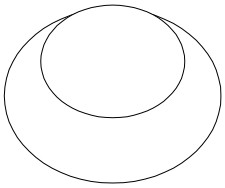
Objectives:

1) Describe the mission and purpose of the Texas Neural Tube Defect Project.
2) Describe two unique methods used in the design and conduct of the border case-control study of neural tube defects.
3) Identify three possible risk factors from the border case-control study of neural tube defects.

Outline:

1) Describe the methods for case control study
2) Descriptive epidemiology of case control population
3) Early findings from the lab component of the study
4) In depth discussion of insulin/obesity and NTDs

Texas Neural Tube Defect Project



Closing the Gap

Neural Tube Defects (NTDs)

- Anencephaly
- Spina bifida
- Encephalocele

Texas Neural Tube Defects Project

Suspected NTD Risk Factors

- Diabetes mellitis
- Hypothermia
- Alchohol consumption

Suspected NTD Risk Factors - Drugs

- Valproic acid
- Carbamazepine
- Retinoic Acid
- Methotrexate

Suspected NTD Risk Factors - Chemicals

- Industrial solvents
- Heavy metals
  - Cadmium
  - Arsenic
- Pesticides

NTD Risks

- **Occurrence risk**
  about 1/1000 live births
- **Recurrence risk**
  about 1/20 live births

Evidence for Genetic Component for NTDs

- More affected females than males
- Ethnic and geographic variation
- Recurrence risks higher than occurrence risks
- Genetic variability with no simple mode of inheritance (multifactorial inheritance)
- Family studies indicate increased risk for near relatives

NTD Rates* by Ethnicity

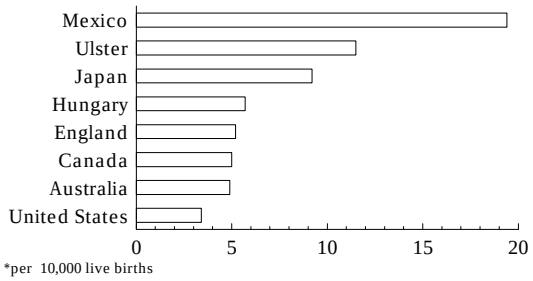
Black	5
Non-hispanic white	10
Hispanic	13 - 16

*per 10,000 live births

Texas Neural Tube Defects Project

NTD Prevalence - Selected Countries

Average Rate* of Anencephaly, 1980-1988



*per 10,000 live births

Folic Acid

- Isolated from spinach leaves and named folic acid (folium means leaf).
- B-vitamin.
- Humans cannot synthesize folic acid and are dependent on dietary sources.

Demographics of Texas-Mexico border counties, 1997

County	Population	% Hispanic	Below Poverty Rank (%)	Births
Cameron	316,542	84	236 (35%)	7,639
Hidalgo	511,324	88	243 (38%)	13,074
Webb	184,980	93	234 (35%)	5,143
El Paso	683,657	73	224 (28%)	14,473
Other 10	175,880	83	--	3,881
Total Border	1,872,383	81	(36%)	44,210
Total Texas	19,384,453	23	(16%)	333,829

Neural Tube Defects Project - Case-control Study

Surveillance

- Target area: 14 Texas-Mexico border states
- 360 resident NTD-affected births
- Overall border NTD rate: 13.4 per 10,000 live births
- 360 with known gestational age
  - 68 (19%) induced or aborted at < 20 weeks;
  - 94 (36%) from 20-33 weeks;
  - 198 (55%) delivered at $\geq$ 34 weeks

Texas Neural Tube Defects Project

Casefinding

- Active surveillance sources

Hospitals - 22	Licensed abortion centers - 4
Birthing centers - 39	Prenatal clinics - 30
Outpatient ultrasound centers - 74	Genetic services providers - 4
Licensed certified nurse midwives - 45	Documented midwives - 103

- Hospital charts, logs, and ICD-9 based searches
- Physician surveys and vital records
- Surveillance teams were located in Cameron, Webb, and El Paso counties

Neural Tube Defects Project - Surveillance

Purpose

Identify risk factors for NTD occurrence

- Case control component of the NTD Project began June 1, 1995
- To date, 364 case and control women who reside in the 14 border counties have been enrolled

Neural Tube Defects Project - Case-control Study

Case-women

- Diagnosis of anencephaly (740.0), spina bifida (741.0), or encephalocele (742.0)
- Delivered in one of the 14 Texas-Mexico border counties
- From June 1995 through February 1999

Neural Tube Defects Project - Case-control Study

Control-women

- Same time-period and residency requirements as cases
- Normal, live births
- Randomly selected in proportion to live births at a facility during the previous year

Neural Tube Defects Project - Case-control Study

Mother questionnaire

- Tobacco
- Alcohol
- Substance abuse
- Environment
- Occupation

Neural Tube Defects Project - Case-control Study

Mother questionnaire (continued)

- Maternal health
- Reproductive history
- Family demographics and medical history
- Nutritional supplements
- Stress and social support

Neural Tube Defects Project - Case-control Study

Laboratory tests on mother's blood

- RBC folate, serum folate and B_{12}, and hypersegmented PMNs
- $HgbA_1C$, glucose, and insulin
- CBC and ferritin
- Sphingasine and sphingonine
- HDL/LDL/total cholesterol and triglycerides

Laboratory tests on mother's blood (cont'd)

- Folate binding protein gene (paternal too)
- PCBs
- Lead
- Arbovirus serology
- Lymphocyte nutritional assay

Laboratory tests on mother's stool/urine

- Ova and parasites
- Arsenic
- Mercury
- Paranitrophenol

Laboratory tests on infant's blood

- RBC folate, serum folate and B_{12}
- Folate and B_{12} metabolites
- HDL/LDL/total cholesterol, and triglycerides

Maternal Indices of Nutritional Status

		Cases		Controls		
Test	Units	N	Mean	N	Mean	p-value
Serum folate	ng/mL	107	18.4	109	12.6	0.75
RBC folate	ng/mL	104	332.0	108	338.0	0.31
Serum B_{12}	pg/mL	107	494.0	109	649.0	0.008
Ferritin	ng/mL	121	36.1	118	41.9	0.04

Fetal Indices of Nutritional Status

		Cases		Controls		
Test	Units	N	Mean	N	Mean	p-value
Serum folate	ng/mL	11	29.6	92	40.9	0.24
RBC folate	ng/mL	6	318.0	52	435.0	0.08
Serum B_{12}	pg/mL	11	414.0	92	582.0	0.04

Maternal Serum - Lipids

		Cases		Controls		
Lipid	Units	N	Mean	N	Mean	p-value
Cholesterol	mg/dL	31	186	43	185	0.77
HDL	mg/dL	25	54	38	48	0.009
LDL	mg/dL	25	114	38	105	0.59
Triglycerides	mg/dL	31	125	43	12	0.74

Neural Tube Defects Project - Case-control Study

Fetal Serum - Lipids

		Cases		Controls		
Lipid	Units	N	Mean	N	Mean	p-value
Cholesterol	mg/dL	12	128	82	78	0.0003
HDL	mg/dL	10	41	67	31	0.80
LDL	mg/dL	9	71	64	41	0.0003
Triglycerides	mg/dL	11	77	80	47	0.09

Neural Tube Defects Project - Case-control Study

Maternal Stool - O&P

	Cases		Controls		
Commensal parasites	Y	N	Y	N	p-value
Blastocystis hominis	20	41	18	35	0.89
Dientamoeba fragilis	0	61	2	51	0.21
Entamoeba hartmanni	3	58	4	49	0.42
Endolimax nana	12	48	3	50	0.03
Entamoeba coli	5	56	1	51	0.14
Iodamoeba buetschlii	3	58	0	52	0.15

Neural Tube Defects Project - Case-control Study

Maternal Stool - O&P

	Cases		Controls		
Pathenogenic parasites	Y	N	Y	N	p-value
Entamoeba histolytica	1	60	0	53	0.53
Giardia lamblia	1	60	0	53	0.53
Hymenolepis nana	3	58	0	53	0.15

Neural Tube Defects Project - Case-control Study

Selected Risk Factors for NTDs

- Insulin-dependent diabetes mellitis (IDDM) — 16-fold risk
- Non-insulin-dependent diabetes mellitis — 2-fold risk
- Obesity — 2-fold risk

Texas Neural Tube Defects Project

Prevalence of DM, Obesity, and NTDs on the Texas-Mexico Border

- NIDDM is 2-3 times higher in Hispanics than in non-Hispanic whites
- Over half of Mexican American women in Texas are overweight
- Risk of NTDs is 50-200% higher in Mexican American women than in non-Hispanic whites

Questionnaire Addressed

- Body mass index (BMI) based on self-reported prepregnancy height and weight
- History of diabetes ("Were you ever told by a doctor that you had diabetes or high blood sugar?")

Neural Tube Defects Project - Case-control Study

Questionnaire Addressed

- Maternal age
- Education
- Income
- Use of alcohol, tobacco, and supplements

Neural Tube Defects Project - Case-control Study

Laboratory Evaluation

- Hgb A1c: whole blood with EDTA tested by ion exchange chromatography at SKB*
- Serum insulin levels: serum tested by a solid-phase I^{125} radioimmunoassay at UTHSC/SA
- Serum glucose levels: serum tested by spectrophotometry at SKB*

*Smith-Kline Beecham

Neural Tube Defects Project - Case-control Study

Analysis

- Univariate logistic regression for each measure
- Categorized into quartiles
- Odds ratios calculated with first quartile as referent
- Multiple logistic regression used to adjust for known risks and risks of interest

Neural Tube Defects Project - Case-control Study

Demographic Characteristics of Study Mexican American Women

	Cases (n = 104) Number	%	Controls (n = 111) Number	%
Maternal Age				
< 20	28	26.9	30	27.0
20 - 24	37	35.6	33	29.7
25 - 29	25	24.0	27	24.3
30+	14	13.5	21	18.9
Education				
< 7 years	25	24.0	14	12.6
7 - 11 years	29	27.9	40	36.0
12+ years	50	48.1	57	51.4

Neural Tube Defects Project - Case-control Study

Demographic Characteristics of Study Mexican American Women

	Cases (n = 104) Number	%	Controls (n = 111) Number	%
Income				
≤ $10K	50	49.5	48	43.6
$11 - $15K	18	17.8	20	18.2
$16 - $25K	18	17.8	20	18.2
> $25K	15	14.9	22	20.0
Country of Origin				
Mexico	53	51.0	57	51.4
US	51	49.0	54	48.7

Neural Tube Defects Project - Case-control Study

Maternal Fasting Glucose, Hgb A1c, Serum Insulin Levels, and BMI

	Glucose	Hgb A1c	Insulin	BMI*
Cases				
N	92	97	104	104
Mean	91.7	5.0	17.1	26.3
Controls				
N	100	99	111	111
Mean	87.4	5.1	12.8	24.7

*Statistically significant mean difference between case and control women at $p < 0.05$

Neural Tube Defects Project - Case-control Study

NTD Risk According to Quartiles of Glucose, Hgb A1c, Insulin, and BMI

	Q1	Q2	Q3	Q4
Glucose (mg/dL)				
OR	1.00	0.80	0.93	1.31
95% CI	referent	0.34-1.87	0.41-2.13	0.59-2.92
Hbg A1c (%)				
OR	1.00	0.55	0.32	0.41
95% CI	referent	0.26-1.17	0.14-0.74	0.19-0.92
Insulin (µIU/mL)				
OR	1.00	1.33	1.70	2.98
95% CI	referent	0.55-3.20	0.71-4.08	1.33-6.68
BMI (kg/m^2)				
OR	1.00	0.98	1.07	1.70
95% CI	referent	0.45-2.13	0.50-2.30	0.81-3.58

Neural Tube Defects Project - Case-control Study

NTD Risk for Insulin Quartiles Stratified by BMI[1] Category

	Insulin Quartile			
	Q1	Q2	Q3	Q4
BMI (kg/m^2) < 27.5				
OR	1.00	1.67	1.71	2.35
95% CI	referent	0.67-4.15	0.67-4.37	0.91-6.07
BMI (kg/m^2) > 27.5				
OR	1.00	----	----	----
95% CI	referent	----	----	----

[1]BMI quartiles 1,2,3 were combined (> 27.5).

Neural Tube Defects Project - Case-control Study

Separating Insulin[1] / BMI[2] Effects

	Per Unit Increase		Q4 vs Q1	
	OR	95% CI	OR	95% CI
Crude				
Insulin Quartiles	1.45	1.13-1.85	3.02	1.44-6.36
BMI (< 27.5, > 27.5)	1.67	0.91-3.06		
Adjusted for insulin or BMI				
Insulin adjusted for BMI	1.14	1.07-1.85	2.79	1.23-6.31
BMI adjusted for insulin	1.17	0.60-2.29		
Adjusted for all other variables[3]				
Insulin	1.41	1.06-1.87	2.78	1.19-6.51
BMI	1.33	0.64-2.76		

[1]A linear logistic relationship was assumed for quartiles of insulin.

[2] BMI, quartiles 1,2,3 were combined and compared to quartile 4 (>27.5)

[3]Age, education , income, smoking, alcohol, vitamin use, and previous pregnancy loss

Neural Tube Defects Project - Case-control Study

Speaker: Russell Larsen, Ph.D.

Topic: Interim Findings from the NTD Recurrence Prevention Study on the Texas-Mexico Border

Objectives:

1) Describe the public health importance of the NTD recurrence prevention project on the Texas side of the Texas-Mexico border.
2) Describe how subjects were enrolled and followed in this study
3) Describe some interim results from this study.

Outline:

1) Objectives
   a) Identify women who have had NDT-affected pregnancies
   b) Educate, counsel, and provide these women with folic acid
   c) Follow subsequent pregnancies
   d) Answer question: Is folic acid protective for Hispanic women?
2) Effective dosage of folic acid protective for Hispanic women?
   a) Dietary supply and fortification inadequate at present
   b) During contraception daily multivitamin (0.4 mg folic acid) necessary
   c) Prior to conception high-dose (4.0 mg) folic acid dose pacs supplied
3) Interim results of intervention
   a) Enrollment status and participation of high risk women in intervention, 1993-1998
      i) Establish eligibility-residence, consent, fecundity
      ii) Natural outcomes of index pregnancy vs. induced abortions
   b) Subsequent pregnancy outcomes
   c) Significance of results
      i) Interim finding-folic acid appears to reduce the risk of NTD recurrence in Hispanic women
      ii) Timely and active NTD surveillance system is necessary
      iii) Need for physicians to educate high and low risk women about benefits of folic acid before conception

Abstract: The primary objective of the Texas Neural Tube Defect Project (TNTDP) was (and is) prevention of recurrent NTDs through provision of folic acid to high risk women who had had an NTD-affected pregnancy and were residents of the 14 Texas-Mexico border counties. If the enrollees were contracepting, they were given a multivitamin with 0.4 mg folic acid; if they were not, they were given daily dosepacs consisting of 4.0 mg folic acid.

Pregnancy outcomes subsequent to the index NTD-affected pregnancy were followed for the period 1993-1998**.** Excluding miscarriages and pregnancies lost to follow-up, only one of 124 pregnancies resulted in a recurrent NTD, rather than the three to five that would have been expected based on a 3-4% recurrence rate ($p = 0.10$-0.18).

The case-woman who had a recurrence repeatedly declined to meet with the field teams and was never able to be apprized of the efficacy of, or provided with, folic acid. This reflects a program failure rather than a folic acid failure. Folic acid appears at this point to reduce the risk of NTD recurrence in Hispanic women, underscoring the importance of a timely and active NTD surveillance system (including fetuses less than 20 weeks gestational age) for population-based and individual NTD prevention. This result also highlights the need and importance for physicians to educate their high and low risk patients about the benefits of folic acid.

Speaker: Russell Kirby, Ph.D., M.S., F.A.C.E.

Topic: The Prevention of Neural Tube Defects from a National Perspective

Objectives:

1) Describe the purpose and scope of the National Birth Defects Prevention Network.
2) Name two NBDPN Activities Focusing on NTD Prevention and Surveillance
3) State the estimated rates of two types of NTDs in the U.S.
4) Summarize opportunities for nationwide prevention initiatives.

Outline:

1) The National Birth Defects Prevention Network
   a) History
   b) Purpose
   c) Current and planned activities in NTD prevention
2) Epidemiology of NTDs
   a) Trends over time
   b) Regional variation
   c) Role of surveillance methodologies
3) Problems in NTD surveillance
4) Opportunities for prevention

Abstract: This presentation will provide a national perspective on prevention of neural tube defects across the United States. The purpose, scope, current and planned activities of the National Birth Defects Prevention Network will be described, with a focus on neural tube defects surveillance and prevention. Trends and spatial variation in prevalence of neural tube defects will be presented. Problems inherent in monitoring neural tube defects nationally will be discussed, and the session will conclude with a review of current and forthcoming national initiatives for prevention of neural tube defects.

The Prevention of Neural Tube Defects: A National Perspective

Russell S. Kirby, PhD, MS, FACE
Department of Obstetrics and Gynecology
Milwaukee Clinical Campus
University of Wisconsin Medical School

Objectives

- **Provide a national perspective on prevention of neural tube defects across the U.S.**
- **Describe the purpose, scope, current and planned activities of the National Birth Defects Prevention Network**
- **Discuss recent trends in prevalence of neural tube defects**
- **Identify problems inherent in monitoring neural tube defects**
- **Review current and forthcoming national initiatives for prevention of neural tube defects**

The National Birth Defects Prevention Network

MISSION STATEMENT: "The mission of the National Birth Defects Prevention Network is to establish and maintain a national network of state and population-based programs for birth defects surveillance and research to assess the impact of birth defects upon children, families, and health care; to identify factors that can be used to develop primary prevention strategies; and to assist families and their providers in secondary disabilities prevention."

History

- **While there were a few pioneering endeavors, birth defects surveillance programs in the US began following the thalidomide scare in the early 1960s, with the creation of the Metropolitan Atlanta Congenital Defects Program (MACDP) in 1967.**
- **By the early 1980s, there were programs in several states. CDC initiated a series of occasional national conferences to bring together birth defects surveillance staff and epidemiologists. A working group defined a minimum dataset (published in Public Health Surveillance, edited by Halperin, Baker and Monson, 1992).**

History (continued)

- **There were several attempts to organize formal activities, including a newsletter. These initiatives typically failed from lack of concerted leadership.**
- **Following the Maternal, Infant and Child Health Epidemiology Program (MICHEP) Workshop in 1996, an informal meeting was held to discuss the formation of an organization to promote birth defects surveillance and prevention in the U.S.**
- **This led to the formation of a steering committee, identification of the name National Birth Defects Prevention Network, and a planning process for a variety of programmatic activities.**

History (continued)

- **The NBDPN was formally organized in 1997. The first annual workshop was held jointly with MICHEP that fall, and the first national birth defects surveillance report was published as an issue of *Teratology* in July/August 1997.**
- **By-laws were developed and approved in 1998, and the first elections of Network officers were held in the fall of 1998.**
- **The second national report has just been released as the January/February 2000 issue of Teratology, and the Network will hold its 3rd annual meeting in New Orleans January 31-February 2, 2000.**

NBDPN Committees

- **Most of the work of NBDPN is accomplished by standing committees. These include:**
  - **committees critical to the functioning of the organization (Executive Committee, Annual Workshop Committee, Data and Annual Report Committee, Newsletter and Communications Committee)**
  - **committees focused on specific tasks or topics (Education and Outreach Committee, Surveillance Guidelines and Standards Committee, NTD Surveillance/Folic Acid Education Committee).**
- **Committee membership is open to all interested members - especially those who roll up their sleeves and get to work!**

OK, You've Convinced Me!

- **How do I join?**
  - **There are currently no barriers to membership in NBDPN other than a willingness to work toward prevention of birth defects through surveillance, research, and programs.**
  - **The member application form and newsletters can be viewed on our website: www.nbdpn.org/NBDPN**
  - **There is also a birth defects surveillance list serv for those interested in sharing ideas or asking questions of interest to colleagues.**

Trends in Prevalence of Neural Tube Defects

- **Prevalence of NTDs varies by race/ethnicity, with significantly higher rates among mothers of Hispanic ethnicity (for all NTDs, anencephalus, spina bifida w/o anencephalus)**
- **Historical data suggests that NTDs show secular trends - rates have been dramatically higher, than lower, in successive eras**
- **Rates may be higher in the southeastern US (based on older data from national hospital discharge surveillance system)**

Trends in Prevalence of Neural Tube Defects (continued)

- **Are prevalence rates declining - and can changes be attributed to recent prevention activities?**
- **There is evidence to suggest that rates are declining. However, surveillance programs vary from state to state, and in many states the programs are of such recency that it is too early to establish trends.**
- **It is too early to gauge the effectiveness of folic acid education and NTD recurrence prevention activities - but don't stop these important programs!**

Surveillance of Neural Tube Defects: Challenges and Opportunities

- **What is the actual prevalence of neural tube defects during a given time period?**
- **What accounts for a change in the prevalence rate?**
  - **random variability?**
  - **decreased exposure to known/unknown teratogens?**
  - **improved antenatal surveillance?**
  - **increased use of pregnancy termination following prenatal diagnosis?**
  - **periconceptional use of folic acid?**
  - **there are very few areas in the US with the capability of trending NTD prevalence for more than 15 years.**

Surveillance of Neural Tube Defects: Challenges and Opportunities (continued)

- **Timeliness of ascertainment: how rapid, how accurate/complete?**
- **Etiologic heterogeneity? Diagnostic heterogeneity!**
- **Variations in birth defects surveillance methods (especially between states, or over time)**
- **Prevention of recurrence of neural tube defects**
- **Use of neural tube defects surveillance data in conjunction with local and statewide public health education/promotion activities**

Activities in Neural Tube Defects Surveillance and Prevention

- **NBDPN has a standing committee focusing on NTD surveillance and folic acid education.**
- **NBDPN is also a member of the National Folic Acid Council.**
- **Committee activities have included a national survey of NTD surveillance methods and use of data in state-level prevention programs (Miller and Kirby, *Teratology* 2000;61:28-32).**

Activities in Neural Tube Defects Surveillance and Prevention (continued)

- **A current project seeks to determine the potential for rapid ascertainment of NTD prevalence.**
- **NBDPN leadership has been closely monitoring NCHS plans to revise the national standard certificate of live birth, with special reference to birth defects reporting.**

Current and Forthcoming National Initiatives for Prevention of Neural Tube Defects

- **Cooperative Agreements between CDC and 18 states to enhance NTD surveillance and recurrence prevention activities**
- **NBDPN project to evaluate potential of state-level rapid ascertainment of NTDs**
- **Opportunities for increased funding for folic acid education, anticipated RFP for additional CDC cooperative agreements this year**

NBDPN - Future Activities

- **Guidelines and Standards for Birth Defects Surveillance Programs**
- **Annual workshops and training seminars**
- **Annual report may evolve into a separate journal or independent publication**
- **The NBDPN website will evolve into a multi-faceted resource for birth defects professionals**
- **Incorporation of NBDPN is in process, enabling the Network to apply for grants and cooperative agreements to further its work**